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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/312,351	05/14/1999	JON A. WOLFF	MIRUS.006	2480
25032	7590	01/05/2006	EXAMINER	
MIRUS CORPORATION			WOITACH, JOSEPH T	
505 SOUTH ROSA RD			ART UNIT	
MADISON, WI 53719			PAPER NUMBER	

1632

DATE MAILED: 01/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/312,351

Applicant(s)

WOLFF ET AL.

Examiner

Joseph T. Woitach

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS; WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 24 October 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 7-11 and 19-28 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 7-11, 19-28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |                                                                                                                        |                                                                                         |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

### **DETAILED ACTION**

This application claims benefit to provisional application 60/085,764, filed May 16, 1998.

Applicants' amendment filed October 24, 2005 has been received and entered. Claims 1-6, 12-18 have been canceled. Claims 7-11, 19-28 are pending and currently under examination.

### ***Specification***

As noted previously, the statement filed May 27, 2005 regarding the sequence listing and CFR has been received and entered.

However, the specification should be amended to reflect the specific SEQ ID NO: for the given sequence. For example page 54, line 18, should be amended to have SEQ ID NO: 1 associated with the poly-glutamic acid recited. Applicant is reminded that 37 CFR 1.821(d) states: "[w]here the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description of claims, even if the sequence is also embedded in the text or the description or claims of the patent application.

The nucleotide sequence disclosure contained in this application fails to comply with 37 CFR 1.821(d). appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-28 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant provide no arguments to the instant rejection, and therefore it is maintained for the reasons of record. As stated previously, the basis of the rejection is a new matter rejection, and addresses whether the instant specification specifically contemplates the claimed invention. In this case, applicants have not pointed to literal support, and as indicated previously a review of the specification by the examiner can not identify literal support for such a limitation. Importantly, none of the possible R groups disclosed provide for a structure with a third thiol group. Examiner does not contest that such groups and/or interactions can exist as evidenced by Applicants' citations, rather these are not contemplated by the teachings of the instant specification.

Again, 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". Claim 24 has been amended to recite "is activated by intramolecular attack from a free thiol such that it is cleaved more rapidly than oxidized glutathione", clearly implying that the third thiol group is comprised on the claimed compound, owever as indicated previously, there is no literal nor structural support

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for such a compound. None of the potential R groups taught recite a third sulfhydryl group is contemplated. Moreover, there is no teaching for providing a compound with the particular property claimed where three thiol groups are present.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 24-28 stand also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described. Again, while similar compounds are known in the art, they are not presented as instantly claimed. As noted previously, there is no specific description nor guidance to what this phrase encompasses, nor how to generate this compound. Further, if a third thiol group existed in the composition for intramolecular attack that would result in a rapid cleavage of a disulfide bond, it is unclear how such a chemical would be made or exist in light of this property.

For the reasons above and of record, the rejection is maintained.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claims 7-11, 19-28 stand rejected under 35 U.S.C. 102(b) as being anticipated by Pierce catalog as evidenced by Arpicco *et al.*

Applicants summarize the basis of the rejection and argue that the limitation of the claims require the functional property of the di-sulfide bond to be maintained “after being linked to molecules on either side” (page 4, first paragraph). Applicants summarize the products provided by the 2004 catalog, argue that particular embodiments are not met by each of these reagents. In each case, Applicants argue that the withdrawing group will be lost when the cross-linking molecule is reacted with other molecules (page 5). See Applicants’ amendment, pages 4-5. Applicants’ arguments have been fully considered, but not found persuasive.

Applicants’ arguments seem to be directed to the intended use of the cross-linker, and not towards the breadth of the claims. At minimum the specification teaches that the structure or core of the claimed molecule of the claimed compound can be R-S-S-R. In view of this, the molecules that are added or modified can be essentially anything, as long as they result in the final product having the functional properties claimed. Applicants do not refute that the cross-linkers have the functional property, only that it is potentially lost if it is reacted with other molecules that would not be electron withdrawing. However, the claimed product must be interpreted as a product obtained by any means, and given its broadest reasonably interpretation for the breadth the claims encompass. In this case, as discussed before, while the method steps are active “forming” steps, a reasonable interpretation of the breadth of the claims is that the composition must simply comprise the labile disulfide, conforming with the R-S-S-R formulation, and meet the functional limitations required by the claims. While the claim is set forth as a product by process, the breadth of the claim for what a reactive group is, the

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requirement for its presence in the final product, and now the claims have been amended to indicate that the molecule is formed with “separate molecules”, no longer requiring that the resulting compound be different at each end. The present specification teaches how to make cross-linking compounds with the recited functional limitation. The broadest reasonable interpretation of the invention as instantly claimed appears to be a homo-bi-functional cross-linker or hetero-bi-functional cross-linker.

The Pierce catalog discloses multiple bi-functional and hetero-bi-functional cross linkers that contain disulfide bonds (pages T-157-T-200). As evidence by Arpicco *et al.* the disulfide bonds of these compounds are more labile and are cleaved more rapidly than glutathione. In light of the minimum requirement that the claimed composition must have a di-sulfide bond that is cleaved more rapidly than glutathione and any other chemical on either side that does not affect this cleavage rate, the hetero-bi-functional cross-linkers anticipate the claims. Since the compounds disclosed by Pierce were synthesized, and thus imply reactable groups were present, they meet the limitations of the claim to encompass reacted groups. As stated previously, assessing what is required and encompassed by the present independent claims it appears that all that is required is a compound with a di-sulfide bond that is cleaved more rapidly than oxidized glutathione. The exact nature of the chemical composition on either side of the di-sulfide bond is broad, but is being interpreted to encompass at least anything that does not affect the ability of the di-sulfide bond to be cleaved more rapidly than glutathione.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is

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appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 7-11 and 19-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 6-8, 10, 11, 19 and 20 of U.S. Patent Application No. 09/75,607, (issue fee now paid).

Although the conflicting claims are not identical, they are not patentably distinct from each other because encompass a complex that comprises a disulfide bond that has a lower thiol pKa than glutathione thiol pKa when measured under the same conditions. Dependent claims set forth the same limitations for the polymer, and that it is capable of attack from a free thiol (claim 19-though also presently subject to an 35 USC 112, first paragraph rejection in the instant application). The intended use for comprising another ligand in the polymer structure, or for the use of delivering a nucleic acid are contemplated and obvious additions to the claimed product in light of the teachings of the present specification

### ***Conclusion***

No claim is allowed.



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**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

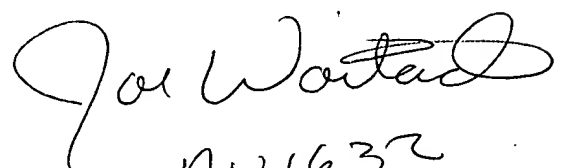
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

  
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